



ACY33316-D4

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: Sridhar Krishna Rabindran et al
Appl. No.:
(Divisional of Serial Number 09/321,182)
Filed: February 28, 2002
Title: REVERSAL OF MULTIDRUG RESISTANCE IN HUMAN COLON
CARCINOMA CELLS

Grp/A.U.:
Examiner:

Docket No: ACY33316-D4

February 28, 2002

Honorable Commissioner of Patents
Washington, D.C. 20231

PRELIMINARY AMENDMENT

Sir:

Preliminary to the examination of the above-identified patent application,
please amend the application as follows:

In the Specification:

Please replace the paragraph beginning at line 18 on page 1 with the following
rewritten paragraph:

- - This application is a divisional application of copending application Serial
Number 09/321,182, filed May 27, 1999 which claims benefit of prior U.S.
Provisional application Number, 60/109,801 which was converted from U.S. Patent
Application Number 09/085,549 filed May 27, 1998, pursuant to a petition filed under
37C.F.R. 1.53(C)(2) on November 2, 1998. These applications are herein
incorporated by reference in their entireties.- -

Please replace the paragraph page 32, lines 12-17 as follows:

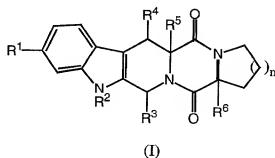
--A viable culture of this new producing strain was deposited with the Culture Collection Laboratory, Northern Utilization Research and Development Division, U.S. Department of Agriculture, Peoria, Ill. on June 7, 1999 and added to its permanent collection under accession number NRRL-30140 in accordance with the Budapest Treaty and is freely available to the public from this depository.--

IN THE CLAIMS

Please cancel Claims 1-12, 29-33, 39-56, 60 and 62 without prejudice.

Amend Claim 57 as follows:

57. (Amended) The method according to claim 13 wherein the chemosensitizing reversal agent is selected from a compound having the Formula (I)



wherein:

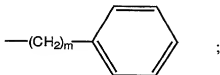
n is an integer of 0, 1, or 2;

R¹ is hydrogen or alkoxy of 1 to 10 carbon atoms;

R² is hydrogen or alkenyl of 2 to 10 carbon atoms;

R³ is hydrogen, alkyl of 1 to 10 carbon atoms, alkenyl of 2 to 10 carbon atoms,

R⁷NH(CH₂)_v— or



m is an integer of 1 to 6;

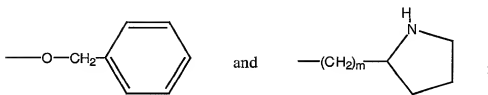
v is an integer of 1 to 4;

R⁴, R⁵ and R⁶ are hydrogen;

R⁷ is H or



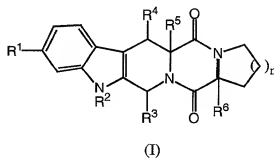
R⁸ is selected from alkyl of 1 to 10 carbon atoms, $\text{---(CH}_2\text{)}_m\text{CO}_2\text{H}$,



or a pharmaceutically acceptable salt thereof.

Amend Claim 58 as follows:

58. (Amended) The method according to claim 18 wherein the chemosensitizing reversal agent is selected from a compound having the Formula (I)



wherein:

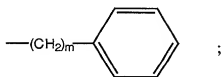
n is an integer of 0, 1, or 2;

R¹ is hydrogen or alkoxy of 1 to 10 carbon atoms;

R² is hydrogen or alkenyl of 2 to 10 carbon atoms;

R³ is hydrogen, alkyl of 1 to 10 carbon atoms, alkenyl of 2 to 10 carbon atoms,

R⁷NH(CH₂)_v– or



m is an integer of 1 to 6;

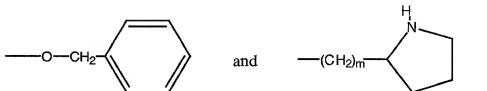
v is an integer of 1 to 4;

R⁴, R⁵ and R⁶ are hydrogen;

R⁷ is H or



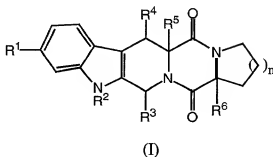
R⁸ is selected from alkyl of 1 to 10 carbon atoms, $\text{—}(\text{CH}_2)_m\text{CO}_2\text{H}$,



or a pharmaceutically acceptable salt thereof.

Amend Claim 59 as follows:

59. (Amended) A method according to claim 24 wherein the chemosensitizing reversal agent is selected from a compound having the Formula (I)



wherein:

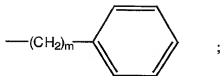
n is an integer of 0, 1, or 2;

R¹ is hydrogen or alkoxy of 1 to 10 carbon atoms;

R² is hydrogen or alkenyl of 2 to 10 carbon atoms;

R³ is hydrogen, alkyl of 1 to 10 carbon atoms, alkenyl of 2 to 10 carbon atoms,

R⁷NH(CH₂)_v— or



m is an integer of 1 to 6;

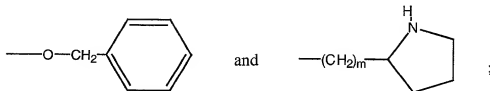
v is an integer of 1 to 4;

R⁴, R⁵ and R⁶ are hydrogen;

R⁷ is H or



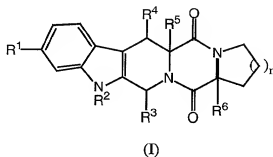
R⁸ is selected from alkyl of 1 to 10 carbon atoms, $-(CH_2)_mCO_2H$,



or a pharmaceutically acceptable salt thereof.

Amend Claim 61 as follows:

61. (Amended) A method according to claim 34 wherein the chemosensitizing reversal agent is selected from a compound having the Formula (I)



wherein:

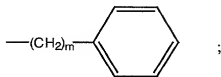
n is an integer of 0, 1, or 2;

R¹ is hydrogen or alkoxy of 1 to 10 carbon atoms;

R² is hydrogen or alkenyl of 2 to 10 carbon atoms;

R^3 is hydrogen, alkyl of 1 to 10 carbon atoms, alkenyl of 2 to 10 carbon atoms,

$R^7NH(CH_2)_v-$ or



m is an integer of 1 to 6;

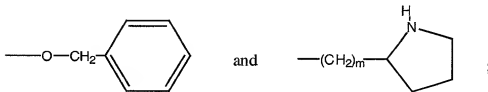
v is an integer of 1 to 4;

R^4 , R^5 and R^6 are hydrogen;

R^7 is H or



R^8 is selected from alkyl of 1 to 10 carbon atoms, $-(CH_2)_mCO_2H$,



or a pharmaceutically acceptable salt thereof.

REMARKS

The present application is a divisional application of U.S. Serial No. 09/321,182. The specification has been amended to reflect the complete prosecution history.

The accession number NRRL-30140 assigned by the Culture Collection Laboratory, Northern Utilization Research and Development Division, U.S. Department of Agriculture, Peoria, Ill. has been added to the specification by amending the specification on page 32, lines 12-17.

Applicants have additionally selected claim 63 to also be prosecuted.

Attached hereto is a marked-up version of changes made to the specification and claims by the current amendment. The attached page is captioned "Version with markings to show changes made."

In view of the foregoing preliminary amendments and remarks, it is respectfully submitted that the present application is in condition for allowance and early notification thereof is earnestly solicited.

Respectfully submitted,



Daniel B. Moran
Registration No. 41,204
Agent for the Applicants

American Home Products
Patent Law Department
5 Giralda Farms
Madison, New Jersey 07940
(845) 602-2224

VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE SPECIFICATION

Paragraph beginning on page 1, line 18 has been amended as follows:

This application is a divisional application of copending application Serial Number 09/321,182, filed May 27, 1999 which claims the benefit of prior U.S. Provisional Application ~~No. Number~~ 60/109,801 which was converted from U.S. Patent Application ~~Number No.~~ 09/085,549 filed May 27, 1998, pursuant to a petition filed under 37 C.F.R. 1.53(c)(2) on November 2, 1998. These applications are herein incorporated by reference in their entireties.

Paragraph beginning on page 32, lines 12-17 has been amended as follows:

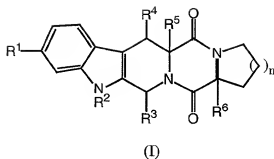
A viable culture of this new product producing stain [will be sent for deposit] was deposited with the Culture Collection Laboratory, Northern Utilization Research and Development Division, U.S. Department of Agriculture, Peoria, Ill. on June [4] 7, 1999 and [will be] added to its permanent collection under accession number [{NRRL- }] NRRL-30140 in accordance with the Budapest Treaty and is freely available to the public from this depository.

IN THE CLAIMS

Claims 1-12, 29-33, 39-56, 60 and 62 have been canceled.

Claim 57 has been amended as follows:

57. (Amended) The method according to claim 13 wherein the chemosensitizing reversal agent is selected from a compound having the Formula (I).



wherein:

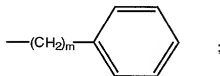
n is an integer of 0, 1, or 2;

R^1 is hydrogen or alkoxy of 1 to 10 carbon atoms;

R^2 is hydrogen or alkenyl of 2 to 10 carbon atoms;

R^3 is hydrogen, alkyl of 1 to 10 carbon atoms, alkenyl of 2 to 10 carbon atoms,

$R^7NH(CH_2)_v-$ or



m is an integer of 1 to 6;

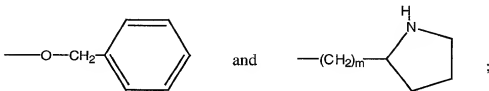
v is an integer of 1 to 4;

R^4, R^5 and R^6 are hydrogen;

R^7 is H or



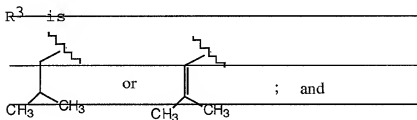
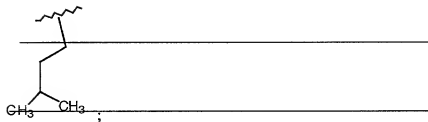
R^8 is selected from alkyl of 1 to 10 carbon atoms, $-(CH_2)_mCO_2H$,



with the proviso that n is not 1 when

a. R^1 is H or CH_3O- ;

R^2 is H or

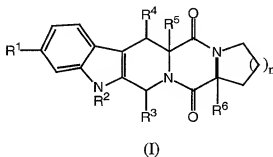


R⁴, R⁵ and R⁶ are hydrogen; and

or a pharmaceutically acceptable salt thereof.

Claim 58 has been amended as follows:

58. (Amended) A method according to claim 18 wherein the chemosensitizing reversal agent is selected from a compound having the Formula (I).



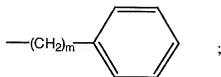
wherein:

n is an integer of 0, 1, or 2;

R¹ is hydrogen or alkoxy of 1 to 10 carbon atoms;

R² is hydrogen or alkenyl of 2 to 10 carbon atoms;

R³ is hydrogen, alkyl of 1 to 10 carbon atoms, alkenyl of 2 to 10 carbon atoms,
R⁷NH(CH₂)_v— or



m is an integer of 1 to 6;

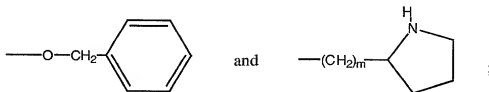
v is an integer of 1 to 4;

R⁴, R⁵ and R⁶ are hydrogen;

R⁷ is H or



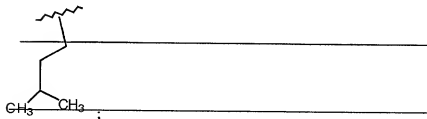
R⁸ is selected from alkyl of 1 to 10 carbon atoms, —(CH₂)_mCO₂H,



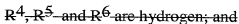
with the proviso that n is not 1 when

a. R¹ is H or CH₃O ;

R² is H or



R³ is _____



Claim 59 has been amended as follows:

59. (Amended) A method according to claim 24 wherein the chemosensitizing reversal agent is selected from a compound having the Formula (I).

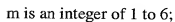


n is an integer of 0, 1, or 2;

R¹ is hydrogen or alkoxy of 1 to 10 carbon atoms;

R² is hydrogen or alkenyl of 2 to 10 carbon atoms;

R³ is hydrogen, alkyl of 1 to 10 carbon atoms, alkenyl of 2 to 10 carbon atoms,

$$R^7NH(CH_2)_v\text{-- or}$$


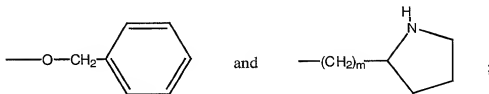
v is an integer of 1 to 4;

R⁴, R⁵ and R⁶ are hydrogen;

 R^7 is H or

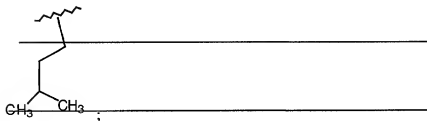


R⁸ is selected from alkyl of 1 to 10 carbon atoms, $-(CH_2)_mCO_2H$,



~~with the proviso that n is not 1 when~~

a. ~~R^1 is H or CH_3O ;~~

 ~~\mathbb{R}^2 is H or~~

\mathbb{R}^3 is _____

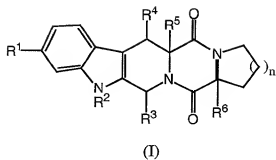


~~R⁴, R⁵ and R⁶ are hydrogen; and~~

or a pharmaceutically acceptable salt thereof.

Claim 61 has been amended as follows:

61. (Amended) A method according to claim 34 wherein the chemosensitizing reversal agent is selected from a compound having the Formula (I).



wherein:

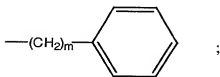
n is an integer of 0, 1, or 2;

R¹ is hydrogen or alkoxy of 1 to 10 carbon atoms;

R² is hydrogen or alkenyl of 2 to 10 carbon atoms;

R³ is hydrogen, alkyl of 1 to 10 carbon atoms, alkenyl of 2 to 10 carbon atoms,

R⁷NH(CH₂)_v— or



m is an integer of 1 to 6;

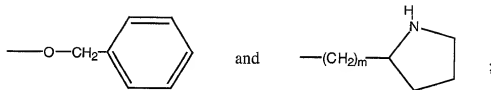
v is an integer of 1 to 4;

R⁴, R⁵ and R⁶ are hydrogen;

R⁷ is H or



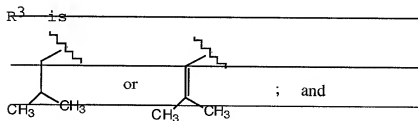
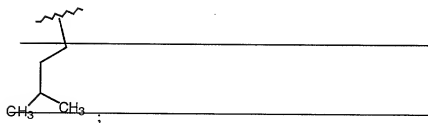
R⁸ is selected from alkyl of 1 to 10 carbon atoms, —(CH₂)_mCO₂H,



with the proviso that n is not 1 when

a. R¹ is H or CH₃O—

R² is H or



R^4 , R^5 and R^6 are hydrogen; and

or a pharmaceutically acceptable salt thereof.